AMENDMENTS TO THE SPECIFICATION

Please replace the Paragraph at page 11, lines 15-18 (published para. [0043]), with the following paragraph rewritten in amendment format:

According to the present invention, translation of the PIRPs during ~~apoptosisresults~~ apoptosis results in production of trophic factors which are released by dying OLs that recruit and promote the survival of remyelinating cells. A similar relationship between dying and surviving cells of OL lineage are predicted to exist during development.

Please replace the Paragraph at page 11, line 27, to page 12, line 2 (published para. [0045]), with the following paragraph rewritten in amendment format:

Specifically, the present invention is directed to an isolated, recombinant [[t]] polypeptide molecule comprising a first amino acid sequence which is a fragment of a native proteolipid protein (preferably mammalian or human PLP/DM20) having a wild type or mutant sequence as compared with the native sequence of said proteolipid protein, and optionally comprising a second amino acid sequence fused in frame thereto to create a fusion polypeptide, which first polypeptide is encoded by an mRNA having an Internal Ribosome Entry-Site [[(]](IRES) wherein translation of the mRNA initiates at said IRES, such that the N-terminal amino acid residue of said first polypeptide corresponds to an internal residue of said proteolipid protein.

Please replace the Paragraph at page 16, line 12, to page 17, line 63 (published para. [0077]), with the following paragraph rewritten in amendment format:

The nucleotide sequence encoding human PLP ~~(SEQ ID NO:1~~ (SEQ ID NO:1) and the full length protein ~~SEQ ID NO:2,~~ (SEQ ID NO:2) are shown below. The stop codon, TGA, is shown. Human genomic DNA includes 3' untranslated segment, the first 16 nucleotides of which are TACACTGGTITCCCTG. Numbering of nucleotides is above, and of amino acid residues is below, the relevant sequences. Annotations are explained following the full length sequence.

FULL LENGTH PLP SEQUENCE (ANNOTATED*)

```
                    15                  30                  45
ATG GGC TTG TTA GAG TGC TGT GCA AGA TGT CTG GTA GGG GCC CCC TTT GCT TCC
Met Gly Leu Leu Glu Cys Cys Ala Arg Cys Leu Val Gly Ala Pro Phe Ala Ser
(0)                  5                  10                  15
                                                    >>>>>>>>>>>

     60                  75                  90                  105
CTG GTG GCC ACT GGA TTG TGT TTC TTT GGG GTG GCA CTG TTC TGT GGC TGT GGA
Leu Val Ala Thr Gly Leu Cys Phe Phe Gly Val Ala Leu Phe Cys Gly Cys Gly
         20                  25                  30                  35
>>>>>>>>>>>>>>>>>>>>>>>>>>> TMD-1 >>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>

            120                 135                 150
CAT GAA GCC CTC ACT GGC ACA GAA AAG CTA ATT GAG ACC TAT TTC TCC AAA AAC
His Glu Ala Leu Thr Gly Thr Glu Lys Leu Ile Glu Thr Tyr Phe Ser Lys Asn
                 40                  45                  50

165                 180                 195                 210
TAC CAA GAC TAT GAG TAT CTC ATC AAT GTG ATC CAT GCC TTC CAG TAT GTC ATC
Tyr Gln Asp Tyr Glu Tyr Leu Ile Asn Val Ile His Ala Phe Gln Tyr Val Ile
     55                  60                  65                  70
                    >>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>> TMD-2 >>>>>>>>>

        225                 240                 255                 270
TAT GGA ACT GCC TCT TTC TTC TTC CTT TAT GGG GCC CTC CTG CTG GCT GAG GGC
Tyr Gly Thr Ala Ser Phe Phe Phe Leu Tyr Gly Ala Leu Leu Leu Ala Glu Gly
               75                  80                  85
>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>

                    285                 300                 315
TTC TAC ACC ACC GGC GCA GTC AGG CAG ATC TTT GGC GAC TAC AAG ACC ACC ATC
Phe Tyr Thr Thr Gly Ala Val Arg Gln Ile Phe Gly Asp Tyr Lys Thr Thr Ile
 90                  95                  100                 105

    330                 345                 360                 375
TGC GGC AAG GGC CTG AGC GCA ACG GTA ACA GGG GGC CAG AAG GGG AGG GGT TCC
Cys Gly Lys Gly Leu Ser Ala Thr Val Thr Gly Gly Gln Lys Gly Arg Gly Ser
        110                 115                 120                 125
                            ****************************************

            390                 405                 420
```

```
AGA GGC CAA CAT CAA GCT CAT TCT TTG GAG CGG GTG TGT CAT TGT TTG GGA AAA
Arg Gly Gln His Gln Ala His Ser Leu Glu Arg Val Cys His Cys Leu Gly Lys
                130                 135                 140
*****************************PLP-specific sequence****************

435                 450                 465                 480
TGG CTA GGA CAT CCC GAC AAG TTT GTG GGC ATC ACC TAT GCC CTG ACC GTT GTG
Trp Leu Gly His Pro Asp Lys Phe Val Gly Ile Thr Tyr Ala Leu Thr Val Val
    145                 150                 155                 160
************************** >>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>

        495                 510                 525                 540
TGG CTC CTG GTG TTT GCC TGC TCT GCT GTG CCC GTG TAC ATT TAC TTC AAC ACC
Trp Leu Leu Val Phe Ala Cys Ser Ala Val Pro Val Tyr Ile Tyr Phe Asn Thr
            165                 170                 175
>>> TMD-3 >>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>

                555                 570                 585
TGG ACC ACC TGC GAC TCT ATT GCC TTC CCC AGC AAG ACC TCT GCC AGT ATA GGC
Trp Thr Thr Cys Asp Ser Ile Ala Phe Pro Ser Lys Thr Ser Ala Ser Ile Gly
180                 185                 190                 195

    600                 615                 630                 645
AGT CTC TGT GCT GAC GCC AGA ATG TAT GGT GTT CTC CCA TGG AAT GCT TTC CCT
Ser Leu Cys Ala Asp Ala Arg Met Tyr Gly Val Leu Pro Trp Asn Ala Phe Pro
        200                 205                 210                 215

            660                 675                 690
GGC AAG GTT TGT GGC TCC AAC CTT CTG TCC ATC TGC AAA ACA GCT GAG TTC CAA
Gly Lys Val Cys Gly Ser Asn Leu Leu Ser Ile Cys Lys Thr Ala Glu Phe Gln
                220                 225                 230

705                 720                 735                 750
ATG ACC TTC CAC CTG TTT ATT GCT GCA TTT GTG GGG GCT GCA GCT ACA CTG GTT
Met Thr Phe His Leu Phe Ile Ala Ala Phe Val Gly Ala Ala Ala Thr Leu Val
    235                 240                 245                 250
                >>>>>>>>>>>>>>>>>>>>>>>>>>>>>>> TMD-4 >>>>>>>>>>>>>>>>>>

        765                 780                 795                 810
TCC CTG CTC ACC TTC ATG ATT GCT GCC ACT TAC AAC TTT GCC GTC CTT AAA CTC
Ser Leu Leu Thr Phe Met Ile Ala Ala Thr Tyr Asn Phe Ala Val Leu Lys Leu
            255                 260                 265
>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>

                825
ATG GGC CGA GGC ACC AAG TTC TGA TACACTCGTTTCCCTG  (SEQ ID NO:1)
Met Gly Arg Gly Thr Lys Phe  (SEQ ID NO:2)
270                 275
```

Please replace the Paragraph at page 21, lines 5-26 (published para. [0086]), with the following paragraph rewritten in amendment format:

The ~~nucleotide~~ nucleotide and amino acid sequences of optimized PIRP-M are shown below and are SEQ ID NO:9 and SEQ ID NO:10, respectively. The nucleotide sequence is annotated and explained below.

PIRP-M (optimized)

```
-10         1               15                  30                  45
GAGCTCCACC ATG TAC GGT GTT CTC CCT TGG AAC GCT TTC CCT GGC AAG GTT TGT
           Met Tyr Gly Val Leu Pro Trp Asn Ala Phe Pro Gly Lys Val Cys

                   60                  75                  90
GGC TCC AAC CTT CTG TCC ATC TGC AAA ACA GCC GAG TTC CAA ATG ACC TTC CAC
Gly Ser Asn Leu Leu Ser Ile Cys Lys Thr Ala Glu Phe Gln Met Thr Phe His

    105                 120                 135                 150
CTG TTT ATT GCT GCG TTT GTG GGT GCT GCG GCC ACA CTA GTT TCC CTG CTC ACC
Leu Phe Ile Ala Ala Phe Val Gly Ala Ala Ala Thr Leu Val Ser Leu Leu Thr

            165                 180                 195
TTC ATG ATT GCT GCC ACT TAC AAC TTC GCC GTC CTT AAA CTC ATG GGC CGA GGC
Phe Met Ile Ala Ala Thr Tyr Asn Phe Ala Val Leu Lys Leu Met Gly Arg Gly

210                 225  (SEQ ID NO:9)
ACC AAG TTC TGA CCG CGG  (SEQ ID NO:10)
Thr Lys Phe ***
```

Please replace the Paragraph at page 21, line 35, to page 22, line 12 (published para. [0088]), with the following paragraph rewritten in amendment format; note that the underlinings of the "CAT" and "His" sequences about position 225 are original to the text and do not indicate an insertion of text:

The sequence below is the His-tagged PIRP-M insert showing a coding sequence that is the same as that shown above but includes a run of 6 His codons at the 3' end. As is well known in the art, the His is added to provide a "tail" that can be bound by certain affinity probes (here, a Nickel column) for purposes of isolation and purification. The His residues and their codons are underscored.

PIRP-M-His (nt sequence is SEQ ID NO:11 and amino acid sequence is SEQ ID NO:12)

```
-10         1               15                  30                  45
GAGCTCCACC ATG TAC GGT GTT CTC CCT TGG AAC GCT TTC CCT GGC AAG GTT TGT
           Met Tyr Gly Val Leu Pro Trp Asn Ala Phe Pro Gly Lys Val Cys
```

```
                  60                  75                  90
GGC TCC AAC CTT CTG TCC ATC TGC AAA ACA GCC GAG TTC CAA ATG ACC TTC CAC
Gly Ser Asn Leu Leu Ser Ile Cys Lys Thr Ala Glu Phe Gln Met Thr Phe His

    105                 120                 135                 150
CTG TTT ATT GCT GCG TTT GTG GGT GCT GCG GCC ACA CTA GTT TCC CTG CTC ACC
Leu Phe Ile Ala Ala Phe Val Gly Ala Ala Ala Thr Leu Val Ser Leu Leu Thr


            165                 180                 195
TTC ATG ATT GCT GCC ACT aTAG TAC AAC TTC GCC GTC CTT AAA CTC ATG GGC CGA GGC
Phe Met Ile Ala Ala Thr Tyr Asn Phe Ala Val Leu Lys Leu Met Gly Arg Gly

210                 225                 240
ACC AAG TTC CAT CAT CAC CAT CAC CAT TGA CCG CGG  (SEQ ID NO:11)
Thr Lys Phe His His His His His His *** (SEQ ID NO:12)
```

Please replace the Paragraph at page 29, lines 6-18 (published para. [0123]), with the following paragraph rewritten in amendment format; note that the underlinings of the "CAT" and "His" sequences about position 225 are original to the text and do not indicate an insertion of text:

The comparison of sequences and determination of percent identity between two sequences can be accomplished using a mathematical algorithm. In a preferred embodiment, the percent identity between two amino acid sequences is determined using the Needleman and Wunsch (J. Mol. Biol. 48:444-453 (1970) algorithm which has been incorporated into the GAP program in the GCG software package (available at ~~http://www.gcg.com~~ www.gcg.com), using either a Blossom 62 matrix or a PAM250 matrix, and a gap weight of 16, 14, 12, 10, 8, 6, or 4 and a length weight of 1, 2, 3, 4, 5, or 6. In yet another preferred embodiment, the percent identity between two nucleotide sequences is determined using the GAP program in the GCG software package (available at ~~http://www.gcg.com~~ www.gcg.com), using a NWSgapdna.CMP matrix and a gap weight of 40, 50, 60, 70, or 80 and a length weight of 1, 2, 3, 4, 5, or 6. In another embodiment, the percent identity between two amino acid or nucleotide sequences is determined using the algorithm of E. Meyers and W. Miller (CABIOS, 4:11-17 (1989)) which has been incorporated into the ALIGN program (version 2.0), using a PAM120 weight residue table, a gap length penalty of 12 and a gap penalty of 4.

Please replace the Paragraph at page 29, lines 19-30 (published para. [0124]), with the following paragraph rewritten in amendment format:

The nucleic acid and protein sequences of the present invention can further be used as a "query sequence" to perform a search against public databases, for example, to identify other family members or related sequences. Such searches can be performed using the NBLAST and XBLAST programs (version 2.0) of Altschul et al. (1990) J. Mol. Biol. 215:403-10. BLAST nucleotide searches can be performed with the NBLAST program, score=100, wordlength=12 to obtain nucleotide sequences homologous to human nucleic acid sequences encoding PLP LMW polypeptides. BLAST protein searches can be performed with the XBLAST program, score=50, wordlength=3 to obtain amino acid sequences homologous to the native protein molecules of the invention. To obtain gapped alignments for comparison purposes, Gapped BLAST can be utilized as described in Altschul et al. (1997) Nucleic Acids Res. 25:3389-3402. When utilizing BLAST and Gapped BLAST programs, the default parameters of the respective programs (e.g., XBLAST and NBLAST) can be used. See ~~http://www.ncbi.nlm.nih.gov~~ www.ncbi.nlm.nih.gov.

Please replace the Paragraph at page 64, lines 5-14 (published para. [0269]), with the following paragraph rewritten in amendment format to state "GATCC"; note that the three occurrences of "AUG" are underlined in the original and are not amendments herein:

To generate the PLP/DM20-M^{205}-CAT fusion constructs, the Bam HI site in the PLP/DM20-GFP M1L plasmids was removed by cutting with Bam HI, fill-in with Klenow Large Fragment, and ligation. A new Bam HI site was introduced upstream of the M^{205} codon by inserting a ~~CATCC~~ GATCC sequence between the G and A of GAAUG. This was accomplished using the QuikChange protocol. This vector, which was termed the pIRES-M^{205} express plasmids, allowed the cloning of PCR fragments into the Met205

triplet via this unique ~~BamHI~~ site. To test this idea, these constructs were cut with Bam HI, blunted with Mung Bean Nuclease, recut with Not I, and ligated to the Not I digested CAT reporter fragment. This PCR fragment was generated using a set of primers that introduced an AAUG sequence at the 5' end (where AUG is CAT initiation codon) and a Not I anchor at the 3' end. Upon ligation, the GAAUG sequence was regenerated and the CAT AUG was placed in the M^{205} context.

Please replace the Paragraph at page 73, lines 22-25, column "b" (published para. [0554]), with the following paragraph rewritten in amendment format:

[263] Garbern, J.Y. (Updated Aug. 16, 2002). PLP-related disorders. In: *GeneReviews* at ~~GeneTests-GeneClinics~~ GeneTests-GeneClinics Medical Genetics Information Resource (database online). Available at ~~http://www.geneclinics.org~~ www.geneclinics.org or ~~http://www.genetests.org~~ www.genetests.org. Accessed 09/12/02.